

Recitation of the Claims

This listing of claims will replace all prior versions and listings of claims in the application:

Claims 1-11 (cancelled)

12. (Amended) A method for generating a secondary library of secondary protein variant sequences of a target protein comprising:

- a) inputting the three dimensional coordinates of said target protein into a computer;
- b) ~~determining a criteria for including favorably ranked primary variant proteins for a primary library;~~
- e) utilizing a force field calculation to generate said a primary library comprising a plurality of favorably ranked primary variant protein sequences comprising variant amino acid residues at variant positions;
- d) ~~determining a criteria for selecting amino acid residues from each of said variant positions from said favorably ranked primary variant proteins~~
- e) c) selecting amino acid residues from a plurality of said variant positions from said favorably ranked primary variant protein sequences; and
- f) d) combining a plurality of said selected amino acid residues to generate said secondary library of said secondary variant protein sequences, wherein at least one of said secondary variant protein sequences is different from said primary variant protein sequences.

13. (Previously presented) A method according to claim 12, wherein said force field calculation is a Self-Consistent Mean Field (SCMF) calculation.

Claims 14-20 (Cancelled)

21. (Previously presented) A method according to claim 12, further comprising synthesizing a plurality of said secondary variant proteins, wherein said combining comprises:

- g) generating a set of oligonucleotide probes each encoding at least one of said amino acid residues at said variant positions;
- h) using said probes in a polymerase chain reaction (PCR) to generate a plurality of oligonucleotide sequences, each encoding said secondary variant sequences; and
- i) producing said secondary variant sequences in host cells transformed with said oligonucleotide sequences.

22. (Previously presented) A method according to claim 21 wherein said PCR is multiple PCR wherein said probes are pooled.

23. (Previously presented) A method according to 22 wherein said probes are added in equimolar amounts.

24. (Previously presented) A method according to claim 22 wherein said probes are combined in amounts that correspond to the frequency of the said amino acid residues at said variant positions in said secondary library.

Claims 25-32 (cancelled)

33. (Previously presented) A method for generating a secondary library of secondary protein variant sequences of a target protein comprising:

- a) inputting the three dimensional coordinates of said target protein into a computer;
- b) ~~determining a criteria for including favorably ranked primary variant proteins for a primary library;~~
- e) utilizing a force field calculation to generate said a primary library comprising a plurality of favorably ranked primary variant protein sequences comprising variant amino acid residues at variant positions;
- d) ~~determining a criteria for selecting amino acid residues from each of said variant positions from said favorably ranked primary variant proteins~~
- e) c) selecting amino acid residues from a plurality of said variant positions from said ~~favorably~~ ranked primary variant protein sequences; and
- f) combining a plurality of said selected amino acid residues from a plurality of said variant positions from said ~~favorably~~ ranked primary variant proteins to generate a secondary library of secondary variant protein sequences.

34. (Previously presented) A method for generating a secondary library of secondary protein variants of a target protein comprising:

- a) inputting the three dimensional coordinates of said target protein into a computer;
- b) ~~determining a criteria for including favorably ranked primary variant proteins for a primary library;~~

e) utilizing a force field calculation to generate said a primary library comprising a plurality of favorably ranked primary variant protein sequences comprising variant amino acid residues at variant positions;

~~d) determining a criteria for selecting amino acid residues from each of said variant positions from said favorably ranked primary variant proteins~~

e) c) selecting amino acid residues from a plurality of said variant positions from said favorably ranked primary variant protein sequences; and

~~f) d)~~ computationally processing a plurality of said selected amino acid residues from a plurality of said variant positions from said favorably ranked primary variant protein sequences to generate a secondary library of secondary variant protein sequences.

35. (Previously presented) A method for generating a secondary library of secondary protein variants of a target protein comprising:

a) inputting the three dimensional coordinates of said target protein into a computer;

~~b) determining a criteria for including favorably ranked primary variant proteins for a primary library;~~

e) utilizing a force field calculation to generate said a primary library comprising a plurality of favorably ranked primary variant protein sequences comprising variant amino acid residues at variant positions;

~~d) determining a criteria for selecting amino acid residues from each of said variant positions from said favorably ranked primary variant proteins~~

e) c) selecting amino acid residues from a plurality of said variant positions from said favorably ranked primary variant protein sequences; and

~~f) d)~~ computationally processing a plurality of said selected amino acid residues from a plurality of said variant positions from said favorably ranked primary variant proteins to generate a secondary library of secondary variant protein sequences, wherein at least one of said secondary variant protein sequences is different from the said primary variant protein sequences.